Norian SRS®
SKELETAL REPAIR SYSTEM®

# Norian® SRS® Cement Reactants Pack Directions for Use

## CAUTION

Federal law (US) restricts this device to sale, distribution, and use by or on the order of a physician who has completed Norian sponsored training in the use of this device.

## DESCRIPTION

Norian SRS Cement is an injectable, moldable, and biocompatible bone cement. The Reactants Pack contains sterile powder (calcium phosphate) and solution (dilute sodium phosphate) components. The Reactants Pack is designed to be placed in a reusable mixer where the 2 components are mixed together to form a smooth, viscous paste that remains injectable for approximately 5 minutes at 18°- 23°C. Norian SRS Cement begins to harden after 2 minutes and sets in approximately 10 minutes at body temperature (37°C). Norian SRS Cement is gradually resorbed over time.

## INDICATIONS

Norian SRS Cement is indicated as an adjunct for fracture stabilization in the treatment of low impact, unstable, metaphyseal distal radius fractures in cases where early mobilization (cast for 2 weeks, then removable splint for 2–4 weeks) is indicated.
Use of SRS alone in highly comminuted fractures is not indicated.

## CONTRAINDICATIONS

Norian SRS Cement should not be used:

- in the presence of active or suspected infection
- in diaphyseal fractures
- as a substitute for external fixation

## WARNINGS

- Do not manipulate site during the 10 minute setting time.
- Do not remove any hardware, including K-wires, until after the device has cured for 24 hours.
- Remove excess material in adjacent soft tissue since the rate of adverse events was higher when extraosseous Norian SRS Cement was present.
- Do not mix Norian SRS Cement with any other substance since this may alter the strength.

## PRECAUTIONS

### *Long Term Effects*

- **The long term effects of extraosseous Norian SRS Cement or intra-articular Norian SRS Cement (material injected into the joint space) are unknown. Arthritis may be a possible complication of intra-articular Norian SRS Cement.**
- **The long term refracture rate of patients with Norian SRS Cement is unknown.**

### *External Fixation*

- **The safety and effectiveness of early removal of external fixation when used with Norian SRS Cement has not been established.**

### *General*

- Familiarity with the surgical principles for cementing fractures, mixing instructions, instrumentation, injection technique, Implant Period, 37°C Work Period, Setting Period and Cure Period are required prior to treatment **(see Figure 1)**.
- Because Norian SRS Cement must be implanted within 5 minutes from the end of mixing, the surgeon should develop a preoperative plan. This requires understanding the method, sequence, and estimated volume of Norian SRS Cement needed to fill the fracture void.
- If more than one Reactants Pack is required, the total volume (not to exceed 40cc) of Norian SRS Cement should be implanted within the 2 minute 37°C Work Period. Disturbing the initial Norian SRS Cement after 2 minutes may damage the construct.
- The Norian SRS Cement Reactants Pack should be equilibrated to 18°–23°C prior to mixing.
- If the Implant Period (5 minutes from end of mixing process) elapses and the Norian SRS Cement has not been implanted into the patient, the remaining paste must be discarded and a new Reactants Pack mixed.
- The safety and effectiveness of Norian SRS Cement in contact with adjacent allograft, acrylic, silicone, or polymer materials has not been established.
- In the event that the seal of the Reactants Pack is breached during mixing, proper eye protection and surgical gloves should be worn when cleaning up the components. Seek medical attention if the components are ingested or inhaled. If skin or eye contact occurs, do the following and seek medical attention if irritation occurs:
  **Skin exposure:** Wash area with soap and water.
  **Eye exposure:** Flush thoroughly with running water.
- Norian SRS Cement is for single use only, and should not be resterilized.
- Unused Norian SRS Cement should be discarded. Before disposal of a Reactants Pack, mix according to the directions for use to render the contents pH neutral.

### *Use in Specific Populations*

The safety and effectiveness of Norian SRS Cement has not been established in:

- multi-fragmentary intra-articular fractures that extend into the diaphysis and/or significant ligamentous disruption (scapholunate instability)
- fractures requiring open surgical reduction or bone grafting
- traumatic open injuries of the injured wrist which are predisposed to infection
- patients with compromised health (e.g., abnormal calcium metabolism, metabolic, vascular, or severe neurological disease, infection, immunologic deficiencies)
- patients who are skeletally immature
- pregnant or nursing women
- patients undergoing concurrent radiotherapy or chemotherapy treatment

## ADVERSE EVENTS

### *Multicenter Clinical Trial*

Norian SRS Cement was investigated in a prospective multicenter clinical trial including a total of 323 patients (161 patients treated with Norian SRS and 162 patients conventionally treated). The adverse events reported to be related to the fracture or treatment are listed in **Table 1.**

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Table 1: Incidence of Complications on Per Patient Basis

| Complication[a] | Norian SRS Cement | | | Control |
|---|---|---|---|---|
| | Total (n=161) | Extraosseous Norian SRS Cement[b] (n=112) | Without Extraosseous Norian SRS Cement (n=49) | Total (n=162) |
| Loss of Reduction[c] | 46 (28.6%) | 41 (36.6%) | 5 (10.2%) | 40 (24.7%) |
| Infection, (pin or K-wire) | 3 (1.9%)[d] | 2 (1.8%) | 1 (2.0%) | 25 (15.4%)[d] |
| Neuropathy[e] | 8 (5.0%) | 6 (5.4%) | 2 (4.1%) | 6 (3.7%) |
| Carpal Tunnel Syndrome[f] | 4 (2.5%) | 4 (3.6%) | 0 (0.0%) | 8 (4.9%) |
| RSD/Sudeck's | 7 (4.3%) | 6 (5.4%) | 1 (2.0%) | 8 (4.9%) |
| Tendinopathy[g] | 6 (3.7%) | 5 (4.5%) | 1 (2.0%) | 6 (3.7%) |
| Tendon Rupture | 6 (3.7%) | 5 (4.5%) | 1 (2.0%) | 2 (1.2%) |
| Infection, osteomyelitis | 1 (0.6%) | 1 (0.9%) | 0 (0.0%) | 0 (0.0%) |
| Pain | 4 (2.5%) | 4 (3.6%) | 0 (0.0%) | 10 (6.2%) |
| Swelling | 2 (1.2%) | 2 (1.8%) | 0 (0.0%) | 1 (0.6%) |
| Intra-articular Norian SRS Cement[h] | 4 (2.5%) | 4 (3.6%) | 0 (0.0%) | NA |
| Other[i] | 9 (5.6%) | 6 (5.4%) | 3 (6.1%) | 13 (8.0%) |
| Total Patient Complications[j] | 100 (62.1%) | 86 (76.8%) | 11 (22.4%) | 119 (73.5%) |
| Total Patients Experiencing ≥ 1 Complication | 74 (46.0%) | 63 (56.3%) | 11 (22.4%) | 82 (50.6%) |

a. Some patients reported more than one complication. For each type of complication, patients are reported with that complication only once.
b. Continued radiographic presence in 29 of 112 patients (26%) at their last visit.
c. There was statistically significantly greater ($p<0.0006$) loss of reduction in the extraosseous Norian SRS Cement group compared to the patients without extraosseous Norian SRS Cement; however, the control patients had statistically significantly greater loss of reduction compared to the Norian SRS Cement patients without extraosseous Norian SRS Cement ($p=0.0301$). The extraosseous Norian SRS Cement group had statistically significantly greater loss of reduction than the control group ($p=0.0336$).

Patients treated with Norian SRS Cement experienced a greater loss of radial length (mean=4.5±4.0 mm) than those treated with conventional fixation (mean=3.7±4.0mm), although this difference was not statistically significant.
d. The proportion of infection was greater for the control patients due to external fixation pin tract infections (18/25); Norian SRS Cement patients did not initially receive external fixation as treatment. Infections were determined by the physician and not necessarily based on cultures.
e. Includes dysesthesia, paresthesia, radial nerve symptoms, ulnar nerve symptoms, and median nerve symptoms. One control patient had a median nerve dysfunction as a pre-existing event.
f. One control patient had carpal tunnel syndrome as a pre-existing condition.
g. Includes tendon weakness, tendonitis, stenosing tenosynovitis, and tendon adhesion.
h. Continued radiographic presence at 12 months in all 4 patients.
i. Includes cellulitis, shoulder bursitis, shoulder impingement, shoulder pain, pin problems, ulna fractures, thumb fracture, ulnar styloid nonunion, fall onto treated wrist, minor trauma to wrist.
j. The proportions of total complications between the total Norian SRS Cement patient population and the control patient population were not statistically significantly different from each other. The proportions of total complications in the extraosseous Norian SRS Cement patients and in the control patients were not statistically significantly different from each other. The proportions of total complications was significantly lower for the Norian SRS Cement patients without extraosseous material compared to patients with extraosseous Norian SRS Cement ($p<0.0001$).

## *Potential Complications*

Other local complications may occur, such as:

- Wound complications such as edema, hematoma, tenderness, redness, and drainage
- Device fracture
- Device migration
- Secondary fractures
- Nonunion or malunion

## MULTICENTER CLINICAL TRIAL

### *Study Design*

A prospective multicenter clinical trial was conducted to evaluate the safety and effectiveness of Norian SRS Cement compared to conventional treatment for low impact, unstable and displaced metaphyseal distal radius fractures.

Randomization

A total of 323 male or female patients were randomized to Norian SRS Cement (161 patients) or control fracture stabilization (162 patients) based on these 4 parameters: fracture type, hand of injury, bone mineral density, and designated treatment method. Patient enrollment was stratified to ensure equal distribution of these 4 parameters, and these were matched between treatment groups.

Designated treatment method was based on the physician's assessment of how they would manage the patient—with external fixation or with a cast. All patients were then randomized. Patients who were randomized to Norian SRS Cement did not receive external fixation. Norian SRS Cement patients who had been originally designated as needing external fixation received a cast and Norian SRS Cement only.

Treatment Method

The use of K-wires was optional for both treatment groups. Norian SRS Cement patients were stabilized using Norian SRS Cement and a cast for 2 weeks, followed by a splint for 2 weeks (20-22 hours per day) to 4 weeks (see Table 2). Patients in the control group received a cast or external fixation for 6–8 weeks. Hand exercises were started at 2 weeks for the Norian SRS Cement patients and at 6–8 weeks for the control patients. The endpoint for evaluation of the functional parameters was 3 months. Patients were evaluated postoperatively through 12 months.

Table 2: Immobilization Time

| Treatment Group | Immobilization Method | Immobilization Time (days) |
|---|---|---|
| Norian SRS Cement | Cast (n=161) | 15.8 ± 5.6 |
| Control | Cast (n=108) | 40.3 ± 12.7 |
| Control | External Fixator (n=54) | 44.8 ± 8.2 |

### *Effectiveness Assessments*

Effectiveness of Norian SRS Cement was determined using functional and radiographic outcomes compared to those of the control group. The primary functional outcome, grip strength, was measured with a dynamometer. The treated limb value was expressed as a percentage of the contralateral. The primary radiographic outcome, loss of radial length, was the difference in radial length between the injured and contralateral radii.

### *Results*

The demographics and baseline characteristics were similar in both treatment groups.

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**Table 3: Patient Characteristics**

| Characteristic | Norian SRS Cement | Control | p-value |
|---|---|---|---|
| Gender [Freq (%)] | | | 0.0447 |
| Female | 129 (80.1%) | 143 (88.3%) | |
| Male | 32 (19.9%) | 19 (11.7%) | |
| Age (years) | | | 0.8945 |
| Mean ±SD | 63.5 ± 11.0 | 63.6 ± 11.5 | |

Extraosseous Norian SRS Cement

There was a 70% (112/161) incidence rate of Norian SRS Cement in the soft tissue adjacent to the fracture site (extraosseous). In all cases, the amount of Norian SRS Cement in the soft tissue diminished over time and completely resorbed in 74% (83/112) of the patients by 12 months, as assessed radiographically.

Primary Outcome—Grip Strength

Although the immobilization time was less for the Norian SRS Cement patients, the grip strength between groups was similar at 3 and 12 months. At 12 months, both groups had 89% of the contralateral grip strength.

Primary Outcome—Radial Length Loss

Norian SRS Cement patients experienced a greater loss of radial length at 3 and 12 months than those treated with conventional fixation, although this difference was not statistically significant based on repeated measures analysis and univariate analysis at these timepoints.

**Table 4: Radial Length Loss**

| Loss of Radial Length | 3 Months | | 12 Months | |
|---|---|---|---|---|
| | SRS | Control | SRS | Control |
| Number of patients | 143 | 143 | 129 | 136 |
| Mean (mm)±SD | 4.7 ± 4.3 | 4.0 ± 4.3 | 4.5 ± 4.0 | 3.7 ± 4.0 |

Designated Treatment Method

There were no differences in grip strength between the treatment groups at 3 and 12 months for either designated treatment method. For mean radial length loss at 12 months, there was a statistically significantly greater loss in Norian SRS Cement patients who had been designated as needing external fixation (mean=4.4±3.8mm) when compared to the control patients who received external fixation (mean=1.9±3.3mm) (p=0.0019 using an unpaired student's t-test). Among patients designated for cast treatment, there were no differences between treatment groups in mean radial length loss at 12 months.

## DIRECTIONS FOR USE (PNEUMATIC MIXER MXR-PNE01-UNV)

1. **Prepare Implant Site:** Remove blood clots and tissue debris; lavage and/or suction instruments may be used. Control active bleeding.
2. **Mix and Load:** Use the Norian Pneumatic Mixer (MXR-PNE01-UNV) to mix the Reactants Pack. Load the Norian Delivery Device (DLD-LRG01-UNV) and attach the Norian Delivery Needle (NDL series).

   ***Note:** If the Norian Pneumatic Mixer (MXR-PNE01-UNV) is not available, the components may be mixed by hand following the Directions for Use for the Norian Mortar and Pestle (MXR-MPS01-UNV).*
3. **Implant Period** (5 minute period at 18–23°C): Norian SRS Cement remains injectable and conformable for 5 minutes. Insert the needle into the operative site and slowly pump the actuation lever to deliver the Norian SRS Cement. Injection of Norian SRS Cement should be performed under direct visualization or under real time image intensification. If obstruction of the needle occurs, the needle should be discarded and replaced with a new needle.

   **PRECAUTION:** If the Implant Period (5 minutes from end of mixing process) elapses and the Norian SRS Cement has not been implanted into the patient, the remaining paste must be discarded and a new Reactants Pack mixed.
4. **37°C Work Period** (2 minute period at 37°C): Norian SRS Cement can be manipulated for 2 minutes from the start of injection in the body. Contour the Norian SRS manually or with an instrument as desired. At body temperature (37°C), Norian SRS Cement begins to set approximately 2 minutes following implantation and may be considered set 10 minutes after implantation is completed.

   **PRECAUTION:** If more than one Reactants Pack is required, the total volume (not to exceed 40cc) of Norian SRS Cement should be implanted within the 2 minute 37°C Work Period. Disturbing the initial Norian SRS Cement after 2 minutes may damage the construct.
5. **Setting Period** (10 minute period at 37°C): Norian SRS Cement should not be manipulated during this10 minute setting period. However, soft tissue closure can proceed provided the Norian SRS Cement in the surgical site is not manipulated in any way.

   ***Note:** If the material has not set in 30 minutes, remove it and start over with a new Reactants Pack.*
6. **Cure Period** (37°C): Norian SRS Cement reaches its ultimate compressive strength by 24 hours.

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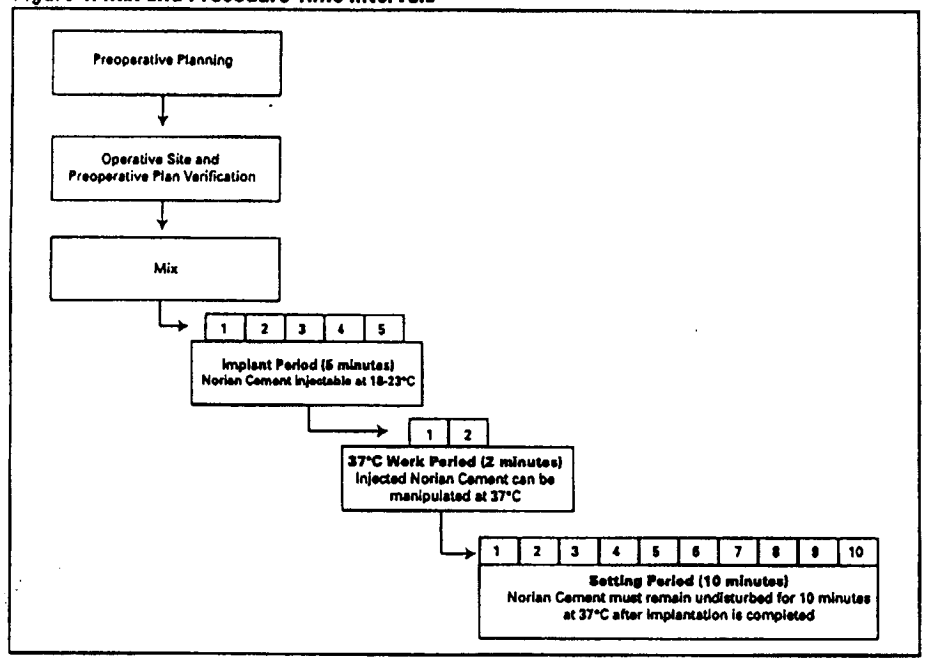
Figure 1: Mix and Procedure Time Intervals




When the Norian Pneumatic Mixer (MXR-PNE01-UNV) is not available, the components may be mixed by hand using the Norian Mortar and Pestle (MXR-MPS01-UNV) which includes a mortar, pestle, and spatula designed specifically for use with Norian Cement. Please reference the Directions for Use below and those included with the Norian Mortar and Pestle (MXR-MPS01-UNV).

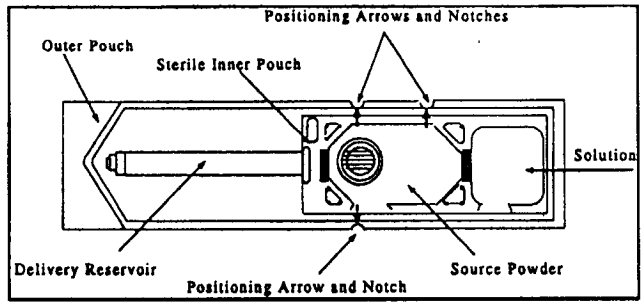
## DIRECTIONS FOR USE (NORIAN MORTAR AND PESTLE MXR-MPS01-UNV)

1. **Empty Powder:** The Norian SRS Cement Reactants Pack should be carefully opened and the powder emptied into the Norian mortar, using aseptic technique.
2. **Mix Solution with Powder:** The solution should be added to the powder and the pestle used to grind the components together at approximately 2 revolutions per second for a total of 2 minutes.
   The ingredients must be mixed for the **entire 2 minutes.** The resultant mix should have a uniform, paste-like consistency with no evidence of unmixed or partially-mixed materials on the mortar or pestle.
3. **Load:** Back-fill the paste into the delivery reservoir supplied in the reactants pack and load the delivery reservoir into the Norian Delivery Device. Attach a Norian Delivery Needle.
4. Follow Directions for Use in previous section, beginning with "3. Implant Period."

## HOW DEVICE IS SUPPLIED

Norian SRS Cement is packaged in a Reactants Pack, which includes the compartment for the Powder, the compartment for the Solution, and the Delivery Reservoir (see Figure 2).
The Norian SRS Cement Reactants Pack is supplied **sterile** and non-pyrogenic. This product is sterilized by gamma irradiation. **Do not resterilize.** This product is intended for Single Use Only. Sterile product packaging should be inspected and if compromised, the product must be assumed non-sterile and appropriately discarded.

Figure 2: Norian SRS Cement Reactants Pack





U.S. Patents: 5,129,905; 5,336,264; 5,569,442; 5,571,493; 5,683,667; 5,709,742; 5,820,632 and others pending
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# Patient Information

# Norian® SRS® Cement Treatment

## Introduction

Norian SRS Cement is a device that is used to help hold the broken bones in your wrist together until they have healed. Norian SRS Cement is used with other devices to stabilize the wrist bones, and must be used by a qualified physician.

## Benefits

With Norian SRS Cement, you may have your cast removed sooner than with other treatments. After your cast is taken off, you will receive a removable splint for 2–4 weeks. This may allow you to move your wrist earlier compared to other treatments.

The material was investigated in a study involving 323 patients with broken wrists. The study investigated the safety and effectiveness of Norian SRS Cement. Each patient was placed into one of two groups. Group I received Norian SRS Cement and then were placed in a cast for 2 weeks. After the cast was removed, they used a removable splint for 2 weeks (20-22 hours per day) to 4 weeks. Group II received standard treatment (a cast or a metal device called an external fixator) and could not move their wrist for 6 to 8 weeks.

## When Norian SRS Cement Should Not Be Used

If you have an infection, Norian SRS Cement should not be used. There are also other cases where Norian SRS Cement has not been determined to be safe and effective, and your doctor is aware of these cases. In addition, if any of the following applies to you, tell your doctor before treatment is started:

- you have a problem with alcohol or drug abuse
- you are pregnant or nursing
- you are undergoing radiotherapy or chemotherapy

## Possible Complications

You may experience complications with Norian SRS Cement. Some of these complications may be the result of the material. Other complications may be similar to types you might also experience with standard treatment.

All of the following serious complications can happen with use of Norian SRS Cement or with standard treatment:

- The broken bone does not heal
- You have limited movement of your wrist after healing
- Bone infection
- Pain
- Redness, swelling, tingling

A potentially serious complication that might occur as a result of using Norian SRS Cement is that the material may get into your wrist joint. It is not known what long term effect the material in your joint may have. One possible long term complication is that you could develop arthritis in the future (approximately 10 years).

In addition, it is possible that your chances of complications may increase if the Norian SRS material gets into the area surrounding the bone and is not removed. In the study, about 70% (112/161) of the patients had small amounts of Norian SRS

Cement (detectable only on x-rays) in the area surrounding the bones. These patients experienced more complications than those patients who did not have Norian SRS Cement in the area surrounding the bone. The material was no longer detectable on x-rays at 1 year in these patients. As a result of the clinical study, your doctor has been trained to remove this excess material.

Also, it is not known whether your bone will be as strong as if you had standard (or other) treatment. In the clinical study, patients with Norian SRS Cement who fell after treatment did not refracture their wrists. However, this group of patients was small, so the chances of you refracturing your wrist if you were to fall after treatment with Norian SRS Cement are not known.

## Commonly Asked Questions

### What is Norian SRS Cement?

Norian SRS Cement is a synthetic material made of ingredients similar to the minerals in bone.

Norian SRS Cement is used to treat broken wrists. The material starts out as a paste that is injected into the broken bones through a small incision. This small incision may require stitches. The paste has a consistency like toothpaste. The paste hardens in your body and helps keep the broken bone in place until the bone has healed. Your doctor will place a cast or other device on your arm to keep your arm from moving after surgery.

Norian SRS Cement is gradually replaced by bone. This occurs through your body's natural bone cell replacement process.

### What other treatments are available?

There are many ways to treat broken wrists, but not all of these options may be suitable for you. Sometimes doctors will choose to use a cast only. Other times, pins may be used in addition to a cast. Another option that doctors may choose is called an external fixator. An external fixator is a metal device that screws into

the bones. Another treatment option is to hold the bone in place with plates and screws and a cast.

Your doctor can explain the risks and benefits of each of these treatment options. Some of these options may not be available to you because of the type and severity of your broken wrist.

## Are there any risks of transmittable diseases with Norian SRS Cement?

No. Because Norian SRS Cement is a man-made material and contains no human or animal by-products, there is no risk of diseases.

## Is Norian SRS Cement toxic?

No. Norian SRS Cement is not toxic.

## Is there anything special I need to do after I have Norian SRS Cement implanted into my wrist?

No. You do not need to do anything special after Norian SRS Cement is injected into your wrist. Your doctor will provide you with detailed instructions on how to take care of your wrist after your operation. The instructions will tell you when you will return to the doctor's office for evaluation after surgery.

In addition, you may have to learn how to care for your cast, pins, or external fixator and return to have the cast, pins or external fixator removed. You will be asked to do hand exercises at home, and you may be asked to see a physical therapist.

When you return to the doctor's office for evaluations, please report any problems that you may have had with your treated wrist.

**If you have questions, please contact your doctor or Norian Corporation at 1-800-966-7153.**